

Appl. No. 09/806,370
Amdt dated July 12, 2004
Reply to Office Action of March 10, 2004

AMENDMENTS TO THE SPECIFICATION

Please insert the attached two (2) page sequence listing after the figures.

Please replace the paragraph on page 38, lines 7-34 with the following paragraph:

The antigenic compositions of this invention also comprise CT-CRM containing at least one additional mutation at a position other than at amino acid residue 29. International application WO 93/13202 (36), which is hereby incorporated by reference, describes a series of mutations in the A subunit which serve to reduce the toxicity of the cholera holotoxin. These mutations include making substitutions for the arginine at amino acid 7, the aspartic acid at position 9, the arginine at position 11, the histidine at position 44, the valine at position 53, the arginine at position 54, the serine at position 61, the serine at position 63, the histidine at position 70, the valine at position 97, the tyrosine at position 104, the proline at position 106, the histidine at position 107, the glutamic acid at position 110, the glutamic acid at position 112, the serine at position 114, the tryptophan at position 127, the arginine at position 146 and the arginine at position 192. The nucleotide sequence encoding the A subunit of the cholera holotoxin is set forth in International application WO 93/13202 (SEQ ID NO: 1). International application WO 98/42375 (37) which is hereby incorporated by reference, describes making a substitution for the serine at amino acid 109 in the A subunit, which serves to reduce the toxicity of the cholera holotoxin. Therefore, using conventional techniques, mutations at one or more of these additional positions are generated.